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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
STEADMAN, DAVID J

ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
04/29/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/076,416	RIEPING ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2008 and 02 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,25-28,33 and 35-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,25-28,33 and 39-42* is/are rejected.

7)☒ Claim(s) *35-38* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 23, 25-28, 33, and 35-42 are pending in the application.

[2] Receipt of a terminal disclaimer, filed on 9/29/08, is acknowledged.

[3] Applicant's response to the Requirement for Information under 37 CFR 1.105, filed on 2/2/09, is acknowledged.

[4] Applicant's arguments filed on 9/29/08 in response to the Office action mailed on 5/27/08, are acknowledged. Applicant's arguments have been fully considered and are deemed to be persuasive to overcome at least one of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

[6] The rejection of claims 23, 25-28, 33, and 39-42 under 35 U.S.C. 103(a) as being unpatentable over Farwick-1, Farwick-2, Farwick-3, Farwick-4, Farwick-5, Burke-1, Burke-2, Burke-3, Burke-4, Burke-5, Hans, Nampoothiri-1, Nampoothiri-2, Nampoothiri-3, Nampoothiri-4, Mockel-1, Mockel-2, Mockel-3, Dusch, Wehmeier, Dunican-1, Dunican-2, Dunican-3, Dunican-4, OR Dunican-5 in view of Kramer, Grabau, Chang-1, and Chang-2 is maintained for the reasons of record and the reasons set forth below.

The rejection was fully explained in a prior Office action. See paragraph 6 beginning at p. 2 of the Office action mailed on 2/2/09.

RESPONSE TO ARGUMENT: At p. 2 of the remarks filed on 9/29/08, applicant attempts to disqualify the primary references as prior art under 35 U.S.C. 102(e) based in-part on the claimed invention being allegedly made by or on behalf of parties to a joint research agreement.

Applicant's argument is not found persuasive because applicant has not perfected the requirement(s) of 35 U.S.C. 103(c)(2)(C), which states "the application for patent for the claimed invention discloses or is amended to disclose the names of the parties to the joint research agreement".

[7] Claim(s) 23, 25-26, 28, 33, and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kikuchi et al. (US Patent 5,932,453; hereafter referred to as "Kikuchi") in view of Shimizu et al. (US Patent 5,445,948; hereafter referred to as "Shimizu") and Chang et al. (*J Bacteriol* 154:756-762, 1983; cited as reference V in the Form PTO-892 mailed on 10/19/05; hereafter referred to as "Chang").

The reference of Kikuchi is cited as teaching methods for producing and collecting L-amino acids, in particular L-lysine and L-threonine, from a culture medium using *E. coli*, including a step of measuring the amount of L-lysine produced (column 9, line 62 to column 10, line 52 and column 15, line 61 to column 18, line 55) and further discloses modified *E. coli* strains that overproduce L-threonine (column 1, lines 34-49). It is noted that by culturing the *E. coli* of Kikuchi to produce L-lysine or L-threonine, the

L-lysine or L-threonine is necessarily concentrated in the medium. The difference between the method of Kikuchi and the claimed method is that the *E. coli* used in the method of Kikuchi does not have an inactivated *poxB* gene.

The reference of Shimizu teaches culturing *E. coli* results in accumulation of acetate in the culture medium (column 3), further teaches that acetate inhibits the growth of *E. coli* in culture (column 4, lines 12-27), and suggests removing the acetate from the culture medium to enhance production of a desired product produced by the *E. coli* (column 6, lines 34-40).

The reference of Chang teaches pyruvate oxidase of *E. coli* catalyzes the decarboxylation of pyruvate to form acetate (p. 756, column 1, top). Chang teaches an *E. coli* mutant with an inactivated *poxB* gene, wherein the gene is inactivated by insertion of a transposon into the *poxB* gene (see, *e.g.,* p. 758, Table 2 and p. 759, right column). Chang teaches culturing of the *E. coli* mutant (see, *e.g.,* p. 756, right column) and the results of Chang indicate that inactivation of the *poxB* gene in *E. coli* is not lethal (see particularly p. 758, left column, middle). According to Chang, growth of *E. coli* on acetate produced by pyruvate oxidase is “feeble” and teaches that preliminary results indicate that most of the endogenous production of acetate is blocked in an *E. coli* strain with an inactivated *poxB* gene (p. 762, column 1, top).

Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to combine the teachings of Kikuchi, Shimizu, and Chang for a method of producing an L-amino acid using an *E. coli* with an inactivated *poxB* gene. One would have been motivated to do this because Shimizu and Chang teach acetate

inhibits growth of *E. coli* in culture and Chang teaches pyruvate oxidase catalyzes the production of acetate, which is blocked in an *E. coli* with an inactivated *poxB* gene. One would have had a reasonable expectation of success for a method of producing an L-amino acid using an *E. coli* with an inactivated *poxB* gene because of the results of Kikuchi, Shimizu, and Chang. Therefore, the method of claims 23, 25-26, 28, 33, and 42 would have been obvious to one of ordinary skill in the art at the time of the invention.

[8] Claim(s) 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kikuchi in view of Shimizu and Chang as applied to claims 23, 25-26, 28, 33, and 42 above and further in view of Matsui et al. (US Patent 4,391,907; hereafter referred to as "Matsui").

The relevant teachings of the references of Kikuchi, Shimizu, and Chang are set forth above. The difference between the method suggested by the combination of Kikuchi, Shimizu, and Chang and the method of claim 27 is that the combined teachings of Kikuchi, Shimizu, and Chang do not teach or suggest L-valine as the desired amino acid for production and isolation.

The reference of Matsui teaches the use of *E. coli* as an L-valine production host (*e.g.,* column 6).

Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to combine the teachings of Kikuchi, Shimizu, Chang, and Matsui to inactivate the *poxB* gene in an *E. coli* for use in production and isolation of L-valine. One would have been motivated to do this because Matsui teaches *E. coli* useful in the

production of L-valine. One would have had a reasonable expectation of success to inactivate the *poxB* gene in an *E. coli* for use in production and isolation of L-valine because of the results of Kikuchi, Shimizu, Chang, and Matsui. Therefore, the method of claim 27 would have been obvious to one of ordinary skill in the art at the time of the invention.

[9] Claim(s) 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kikuchi in view of Shimizu and Chang as applied to claims 23, 25-26, 28, 33, and 42 above and further in view of Dunican et al. (US Patent 6,586,214; hereafter referred to as "Dunican").

The relevant teachings of the references of Kikuchi, Shimizu, and Chang are set forth above. The difference between the method suggested by the combination of Kikuchi, Shimizu, and Chang and the method of claims 39-41 is that the combined teachings of Kikuchi, Shimizu, and Chang do not teach or suggest inactivating the *E. coli poxB* gene by deletion mutagenesis, homologous recombination, and/or transition or transversion mutagenesis.

The reference of Dunican teaches methods for attenuating gene expression, including “transitions, insertions, deletions and transversions” and teaches that such methods are achieved by known prior-art techniques (column 6, lines 17-61). Dunican goes on to teach attenuation by deletion mutagenesis, homologous recombination, and transition or transversion mutagenesis (*e.g.,* claim 1).

Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to combine the teachings of Kikuchi, Shimizu, Chang, and Dunican to inactivate an *E. coli poxB* gene by deletion mutagenesis, homologous recombination, and/or transition or transversion mutagenesis and use the resulting *E. coli* in the method of Kikuchi. One would have been motivated to do this because Dunican teaches such methods are known for gene inactivation and require only routine techniques to practice. One would have had a reasonable expectation of success to inactivate an *E. coli poxB* gene by deletion mutagenesis, homologous recombination, and/or transition or transversion mutagenesis and use the resulting *E. coli* in the method of Kikuchi because of the results of Kikuchi, Shimizu, Chang, and Dunican. Therefore, the method of claims 39-41 would have been obvious to one of ordinary skill in the art at the time of the invention.

Claim Rejections - Double Patenting

[10] The provisional obviousness-type double patenting rejection of claims 23, 25-28, 33, and 39-42 as being unpatentable over claim 7 of co-pending US non-provisional application 10/483,413 is withdrawn in view of the amendment to the claims in the '413 application.

[11] The obviousness-type double patenting rejection of claims 23, 25-28, 33, and 39-42 as being unpatentable over claim 28 of US Patent 7,319,026 is withdrawn in view of the terminal disclaimer filed on 9/29/08.

[12] The provisional obviousness-type double patenting rejection of claims 23, 25-28, 33, and 39-42 as being unpatentable over: 1) claim 44 of co-pending US non-provisional application 10/794,417, claim 22 of co-pending US non-provisional application 10/812,315, and claim 33 of co-pending US non-provisional application 11/350,043 is maintained for the reasons of record and the reasons set forth below. The provisional rejection was fully explained in a prior Office action. See paragraphs 6-7 beginning at p. 7 of the Office action mailed on 5/27/08.

RESPONSE TO ARGUMENT: At p. 3 of the remarks filed on 2/2/09, applicant requests that the provisional rejections be withdrawn and permit the application to issue as a patent. This is not found persuasive since this provisional rejection is not the only remaining rejection in the application.

[13] Claims 23, 25-28, 33, and 39-42 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 40 of copending Application No. 11/658,477. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the above mentioned applications anticipate claims 23, 25-28, 33, and 39-42 herein or the specification of the application supports an embodiment that would anticipate claims 23, 25-28, 33, and 39-42 herein. Claims 23, 25-28, 33, and 39-42 of the instant application cannot be considered to be patentably distinct over the claims of the above mentioned applications when there is a specifically recited embodiment that falls within the scope

of claims 23, 25-28, 33, and 39-42 herein. Alternatively, claims 23, 25-28, 33, and 39-42 cannot be considered to be patentably distinct when there is a specifically disclosed embodiment in the applications that supports the claims and falls within the scope of claims 23, 25-28, 33, and 39-42 herein because it would have been obvious to one of ordinary skill in the art to modify the claimed methods by specifically using an *Escherichia coli* host with an inactivated *poxB* gene. One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within the claims. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

[14] Status of the claims:

Claims 23, 25-28, 33, and 35-42 are pending.

Claims 23, 25-28, 33, and 39-42 are rejected.

Claims 35-38 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/David J. Steadman/
Primary Examiner, Art Unit 1656